510(k) SUMMARY

LIPOSCIENCE

SEP 27 2011

A. 510(k) Number: K111516

B. Submitter Contact Information:

Submitter:
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C. Device Name:

Trade Name: *NMR LipoProfile*® test and NMR Profiler
Common Name: NMR LipoProfile test and NMR Profiler
Classification Names:
Lipoprotein test system, 21 CFR 862.1475, Product Code MRR and LBS
Cholesterol test system 21 CFR 862.1175, Product Code LBS
Triglyceride test system, 21 CFR 862.1705, Product Code CDT
Quality Control material, 21 CFR 862.1660, Product Code JJY
Calibrator, 21 CFR 862.1150, Product Code JIT
Panel: Clinical Chemistry (75)

D. Legally Marketed Device to which Equivalence is Claimed (Predicate Device):

NMR Profiler and NMR Lipoprofile Assay, K063841

E. Device Description:

The *NMR LipoProfile®* test and NMR Profiler involves measurement of the 400 MHz proton NMR spectrum of a plasma/serum sample, deconvolution of the composite signal at approximately 0.8 ppm to produce signal amplitudes of the lipoprotein subclasses that contribute to the composite plasma/serum signal, and conversion of these subclass signal amplitudes to lipoprotein subclass concentrations. The ~0.8 ppm plasma NMR signal arises from the methyl group protons of the lipids carried in the LDL, HDL and VLDL subclasses of varying diameters. The NMR signals from the various lipoprotein subclasses have unique and distinctive frequencies and lineshapes, each of which is accounted for in the deconvolution analysis model. Each subclass signal amplitude is proportional to the number of subclass particles emitting the signal, which enables subclass particle concentrations to be calculated from the subclass signal amplitudes derived from the spectral deconvolution analysis. LDL subclass particle concentrations, in units of nanomoles of particles per liter (nmol/L), are summed to give the reported total LDL particle concentration (LDL-P). By employing conversion factors assuming that the various lipoprotein subclass particles have cholesterol and triglyceride contents characteristic of normolipidemic individuals, HDL cholesterol and triglyceride concentrations are also derived.

SPECIMEN

Types of Specimen

Freshly drawn serum collected in the NMR LipoTube (manufactured by Greiner, Inc. Part #456293) is the preferred specimen. Freshly drawn serum collected in plain red-top blood collection tubes and plasma collected in EDTA or heparin tubes are also acceptable specimens. Serum or plasma specimens drawn in gel barrier collection tubes other than the NMR LipoTube are unsuitable for analysis and should not be used. The optimum specimen volume is ≥0.5 mL. Patient fasting is not necessary prior to the blood draw, except for determination of fasting triglyceride concentrations.

Specimen Storage and Stability

- Specimens collected in the NMR LipoTube should be held upright at room temperature for 20 to 30 minutes and allowed to clot and then refrigerated at 2-8°C. The specimens should be centrifuged within 24 hours of collection and then stored in the original collection tube at 2-8°C for up to 5 days prior to testing.
- It is recommended that blood samples be centrifuged within 6 hours of collection and the serum or plasma removed to a transfer tube and stored at 2-8°C for up to 5 days prior to testing.
- Serum or plasma should not remain at room temperature longer than 6 hours. If assays are not completed within 6 hours, specimens should be stored at 2-8°C for up to 5 days prior to testing.
- Serum or plasma specimens are stable for up to 5 days at 2-8°C. Samples may be frozen at -80°C for up to 5 days prior to testing.

REAGENTS AND MATERIALS

- **Diluent 1** (*NMR LipoProfile*® test) - aqueous solution containing Na_2EDTA (5.0mM), $CaCl_2$ (1.0mM), KCL (120mM), Na_2HPO_4 (50mM), pH 7.4.
- **WASH** (NMR Fluidics System Solution) - Triton X-100-0.1%v/v, Liqui Nox 0.1% v/v in deionized water, pH 10.0.
- **NMR Reference Standard** – 0.2% w/v aqueous solution of Trimethyl Acetate (TMA) disodium salt (15.0 mM) containing Na_2EDTA (5.0 mM), $CaCl_2$ (3.0 mM), KCl (120 nM), D_2O 10% v/v.
- ***NMR LipoProfile*® test Quality Control material** - two levels of pooled human serum-based control material, labeled Control A and Control B, with pre-determined target ranges, containing 0.02% sodium azide as a preservative.
- **NMR Profiler** - 400 MHz proton nuclear magnetic resonance spectrometer interfaced with a liquid sample handler, deconvolution software and provided with a system Operator's Manual.

F. Indications for Use

The *NMR LipoProfile*® test, when used with the NMR Profiler, an automated NMR spectrometer, measures lipoprotein particles to quantify LDL particle number (LDL-P), HDL cholesterol (HDL-C), and triglycerides in human serum and plasma using nuclear magnetic resonance (NMR) spectroscopy. LDL-P and these NMR-derived concentrations of HDL-C and triglycerides are used in conjunction with other lipid measurements and clinical evaluation to aid in the management of lipoprotein disorders associated with cardiovascular disease. This test is performed and provided as a service by LipoScience Laboratory.

G. Technological Characteristics and Substantial Equivalence:

The NMR LipoProfile test, when used with the NMR Profiler is as safe and effective as the previously cleared NMR LipoProfile test and NMR Profiler. The NMR LipoProfile test has the same intended use and indication for use as well as the same principle of operation as the predicate device. The minor technological differences between the NMR LipoProfile test and the predicate device raise no new issues of safety or effectiveness. Performance data further demonstrate that the NMR LipoProfile test is as safe and effective as its predicate device. Thus, the NMR LipoProfile test, when used with the NMR Profiler is substantially equivalent to the predicate device.

Similarity to the Predicate Device

As with the predicate test, the NMR LipoProfile test is intended for the separation and quantification of LDL-P, HDL-C and triglycerides in serum and plasma, measurements

of which are used in conjunction with other lipid measurements and clinical evaluation to aid in the management of lipoprotein disorders associated with cardiovascular disease.

Therefore, substantial equivalence of the NMR LipoProtein test to the claimed predicate device is based upon the following:

1. Both devices have the same intended use and indications for use statements.
2. Both devices use the same clinical test specimen (human serum and plasma).
3. Both devices provide the same analytical test result.
4. Both devices have substantially similar safety and effectiveness when used as intended.
5. Both devices utilize the same signal generation and signal processing algorithm.
6. Both devices have the same reference range.

Differences from the Predicate Device

The NMR LipoProfile test differs from its predicate in two ways:

1. The Gen 2.1 software used with the *NMR LipoProfile*® test and NMR Profiler is a modified version of the predicate software which enhances the curve fit of the software algorithm used for calculating LDL-P results.
2. The modular software architecture utilizes updated Assay Server software and is designed to allow interface with multiple Data Analysis Software that calculates individual analyte values. The modified architecture enables separate modules for analytes which allows for modules to change and new modules to be added with no impact to the signal generation or to other unmodified analytes.

Substantial Equivalence Summary

The proposed *NMR LipoProfile*® test and NMR Profiler is substantially equivalent to the predicate device. There are no significant differences which would affect safety and effectiveness of the proposed device.

H. Performance Data – Non-Clinical:

Analytical Sensitivity

The analytical sensitivity of the NMR LipoProfile test measurements of LDL-P, HDL-C, and triglycerides was determined as the lowest concentration measurable with acceptable precision and accuracy. Serum specimens with low initial concentrations LDL-P, HDL-C, and triglycerides were serially diluted and 20 replicates of each were analyzed. CVs and % bias between observed and target values were determined and acceptance criteria are based on total error ≤20%. Limits of quantification (LOQ) are 300 nmol/L for LDL-P, 10 mg/dL for HDL-C, and 25 mg/dL for triglycerides.

Assay Precision

Within-run precision and within-laboratory precision were determined by testing 20 replicates of three patient serum pools in the same run and in 20 different runs over 20 days. The pools were analyzed according to EP-5A. The results of this testing are summarized below:

Within-run Precision (n=20)

	Pool #1			Pool #2			Pool #3		
	Mean	**SD**	**%CV**	**Mean**	**SD**	**%CV**	**Mean**	**SD**	**%CV**
LDL-P, nmol/L	908	45.4	5.0%	1493	64.8	4.3%	1967*	72.8	3.7%
HDL-C, mg/dL	23.7	0.5	2.0%	54.9*	1.0	1.9%	95.1	0.9	0.9%
Triglycerides, mg/dL	81.0	2.1	2.6%	140.6	2.5	1.8%	649.5	8.7	1.3%

*One replicate of the medium and high pool produced no data resulting in a n=19

Within-Laboratory Precision (n=80)

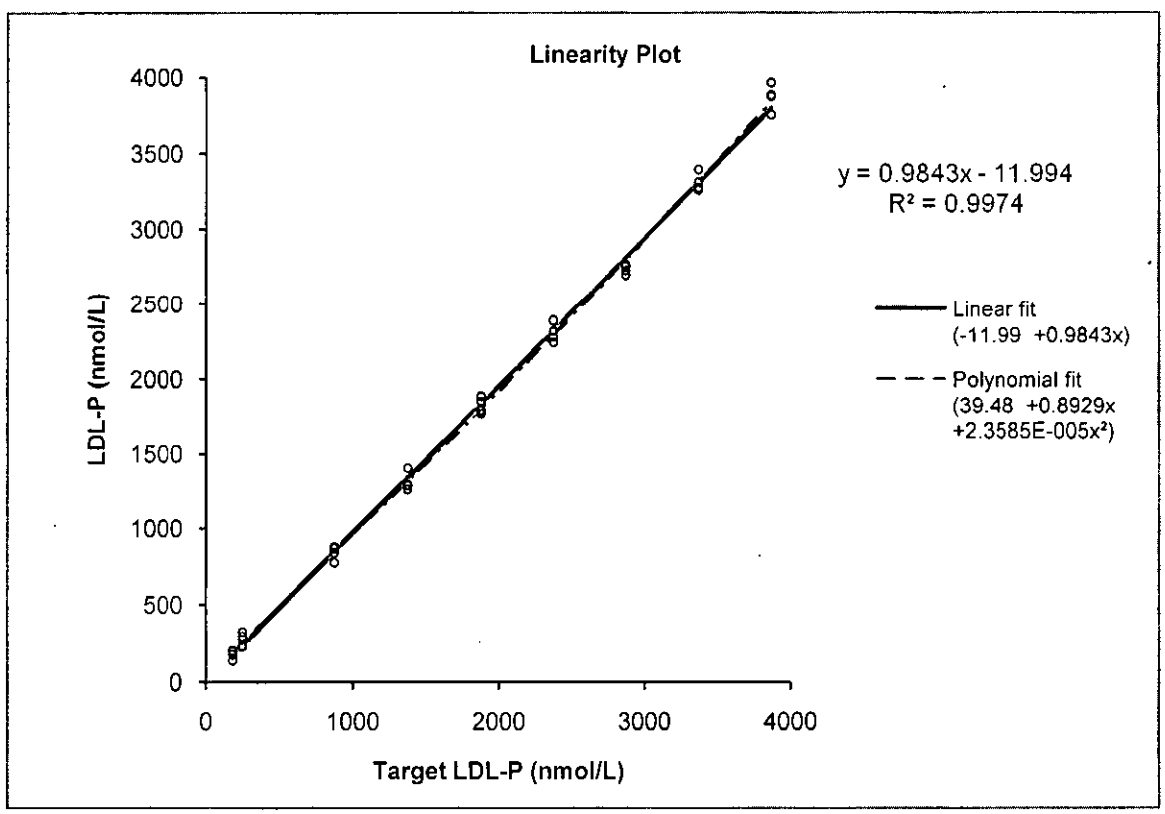
	Pool #1			Pool #2			Pool #3		
	Mean	**SD**	**%CV**	**Mean**	**SD**	**%CV**	**Mean**	**SD**	**%CV**
LDL-P, nmol/L	920.4	70.5	7.7%	1508.3	67.7	4.5%	1991.8	84.6	4.3%
HDL-C, mg/dL	23.7	0.8	3.3%	56.7	1.1	2.0%	96.1	1.7	1.8%
Triglycerides, mg/dL	78.4	2.8	3.6%	145.4	3.7	2.6%	624.6	15.4	2.5%

Linearity

Three serum pools were prepared from patient specimens with low, medium and high values of LDL-P, HDL-C and Triglycerides as determined by *NMR LipoProfile* test. Each were mixed and diluted in different proportions to produce eleven (for LDL-P) or Twelve (12) (TG and HDL-C) different samples with widely varying target concentrations. Mean values from analysis of four replicates of each pool were compared to the expected target values to determine the percent bias for each sample. The serum pools were analyzed according to EP6-A. Tables and regression plots of the linearity data for LDL-P, HDL-P and Triglycerides are given below:

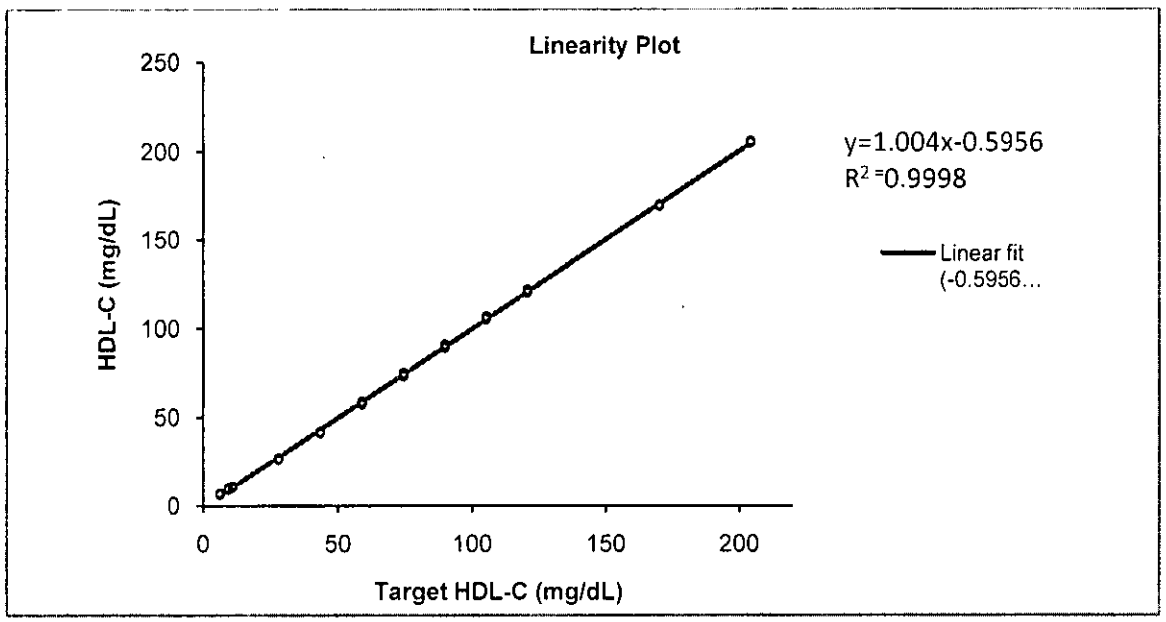
LDL-P Measuring Range: 300-3500 nmol/L

Level	1	2	3	4	5	6	7	8	9
Target value	184.0	247.7	874.2	1373.2	1875.9	2371.1	2870.1	3369.1	3868.0
Observed Mean	179.3	280.3	839.3	1309.8	1825.5	2309.3	2737.8	3309.3	3868.5
Non-linearity	35.4	30.3	-10.5	-29.7	-37.2	-32.9	-16.8	10.9	50.4
Nonlinearity goal	52.1	52.1	87.4	137.3	187.6	237.1	287.0	336.9	386.8



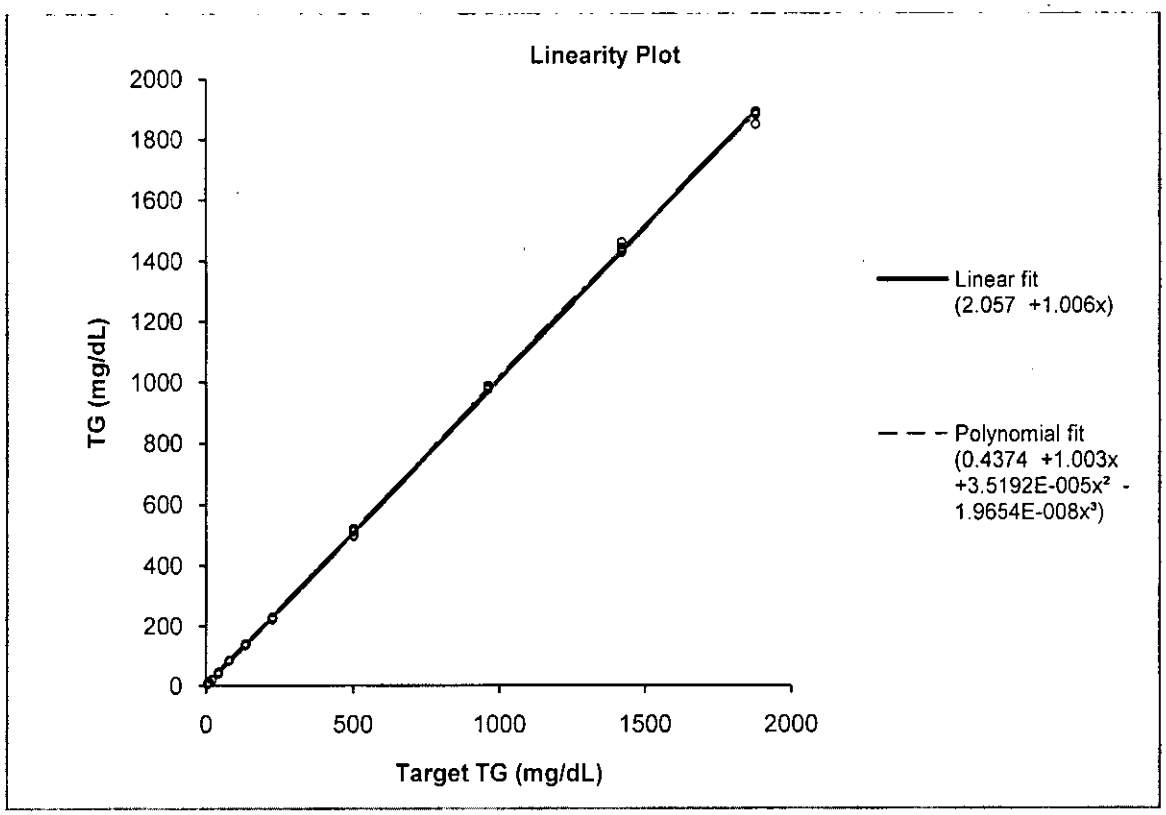
HDL-C Measuring Range: 7-140 mg/dL

Level	1	2	3	4	5	6	7	8	9	10	11	12
Target value	6.3	9.4	10.9	28.0	43.4	59.0	74.4	89.8	105.3	120.8	170.3	204.4
Observed Mean	6.5	9.3	10.8	26.8	41.8	58.0	74.0	90.0	106.0	121.3	169.3	205.3
Nonlinearity goal	0.7	0.9	1.1	2.8	4.3	5.9	7.40	9.0	10.5	12.1	17.0	20.4



Triglycerides Measuring Range: 5-1100 mg/dL

Level	1	2	3	4	5	6	7	8	9	10	11
Target value	5.4	10.9	21.8	43.6	79.5	133.4	223.2	492.7	941.8	1390.9	1840
Observed average	5	11.3	22.1	48.6	88	143.1	232	513.7	964.9	1414	1857
Nonlinearity goal	2.6	2.6	2.6	4.3	8.0	13.5	22.7	50.2	96.2	142.1	188.0



Linear Regression analysis: y=1.006x + 2.057 R^2=0.9998

Interfering Substances

Endogenous substances normally found in blood and exogenous substances (common and prescription drugs) were evaluated for potential interference with the *NMR LipoProfile®* test by LipoScience. Five endogenous agents and twenty two drugs were screened for potential interfering effects to NMR LipoProfile test using concentrations in accordance to CLSI EP7-A2 guidelines.

Endogenous		***Exogenous (OTC drugs, etc.)***	
Potential Interferent	***Test Concentration***	***Potential Interferent***	***Test Concentration***
Hemoglobin	2 mg/mL	Simvastatin	48 µg/mL
Bilirubin, unconj.	200 µg/mL	Fenofibrate	45 µg/mL
Creatinine	50 µg/mL	Nicotinic Acid Sodium salt	1.2 mg/mL
Urea	2.6 mg/mL	Acetylsalicylic acid	652 µg/mL
Uric acid	235 µg/ml	Acetaminophen	200 µg/mL
		Naproxen Sodium	547 µg/mL
		Ibuprofen Sodium salt	210 [1], 70 [2] µg/mL
		Piroxicam	60 µg/mL
		Hydrochlorothiazide	6.0 µg/mL
		Triamterene	8.9 µg/mL
		Pravastatin	48 µg/mL
		Furosemide	60 µg/mL
		Metoprolol tartrate	6.4 µg/mL
		Nifedipine	400 µg/mL
		Enalaprilat Dihydrate	0.3 µg/mL
		Hydralazine hydrochloride	180 µg/mL
		Isosorbide dinitrate (lactose mixture 2:3)	375 µg/mL
		Clopidogrel hydrogensulfate	360 µg/mL
		Glipizide	2.0 µg/mL
		Metformin Hydrochloride	600 µg/mL
		Pioglitazone hydrochloride	27 µg/mL
		Atorvastatin	48 µg/mL

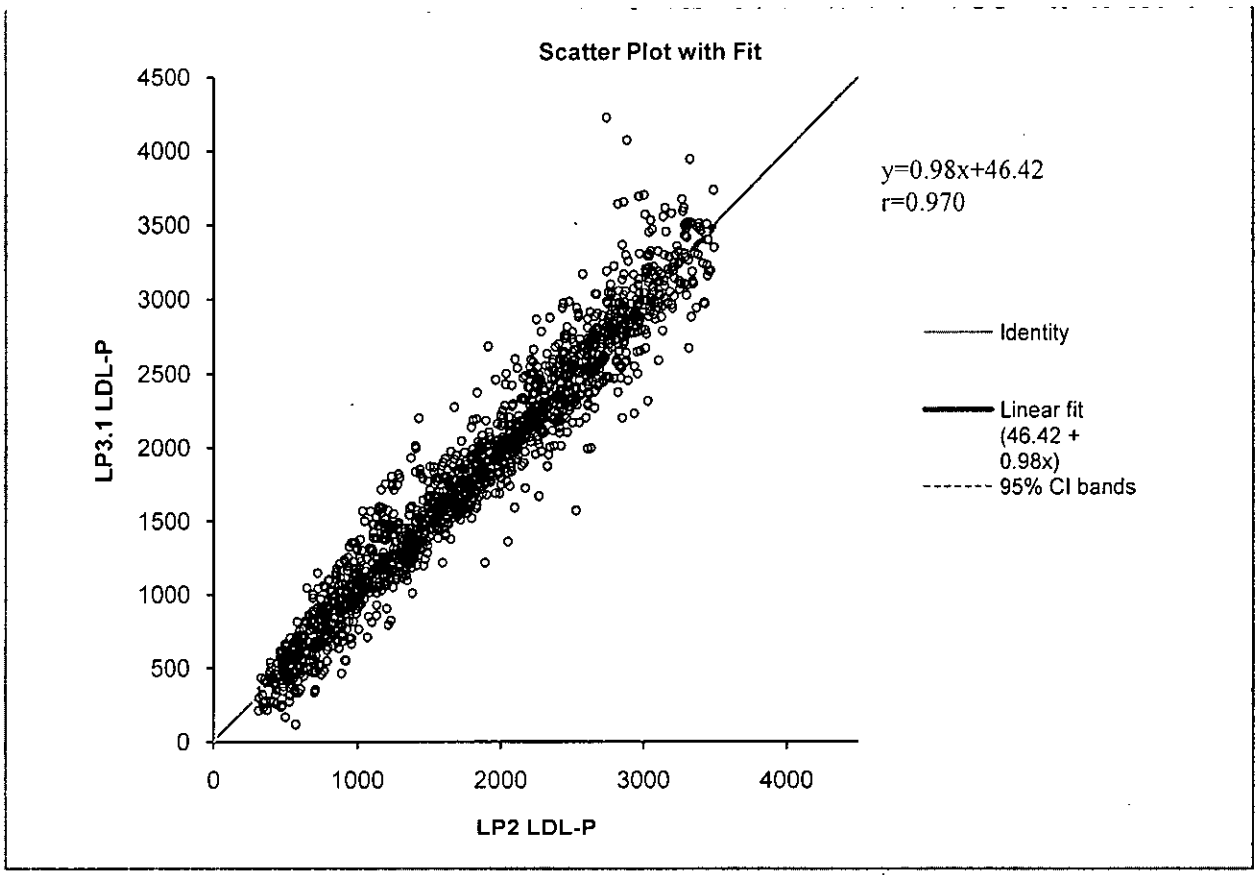
[1] For LDL-P and HDL-C
[2] Test results for triglycerides were ~4 to 6% lower at the 140 and 210 µg/mL concentrations of ibuprofen

H. Method Comparison – Non-Clinical:

Method Comparison – LDL-P

Method comparison was evaluated by using serum samples across the reportable range of the *NMR LipoProfile* test for LDL-P on the NMR Profiler. LDL-P concentrations ranged from 315to 3497 nmol/L.

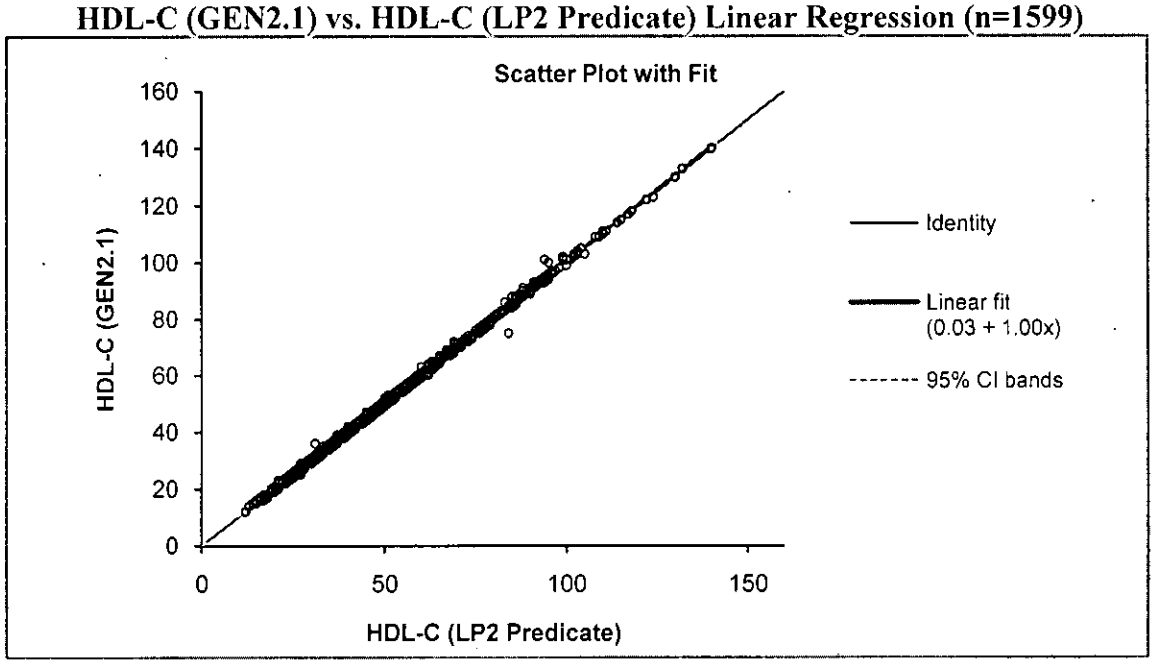
LDL-P (GEN2.1) vs. LDL-P (Predicate) Linear Regression (n=1555)



Method Comparison – HDL-C

Method comparison was evaluated by using serum samples across the reportable range of the *NMR LipoProfile* test for HDL-C on the NMR Profiler. HDL-C concentrations ranged from 12 to 140 mg/dL.

HDL-C (GEN2.1) vs. HDL-C (LP2 Predicate) Linear Regression (n=1599)

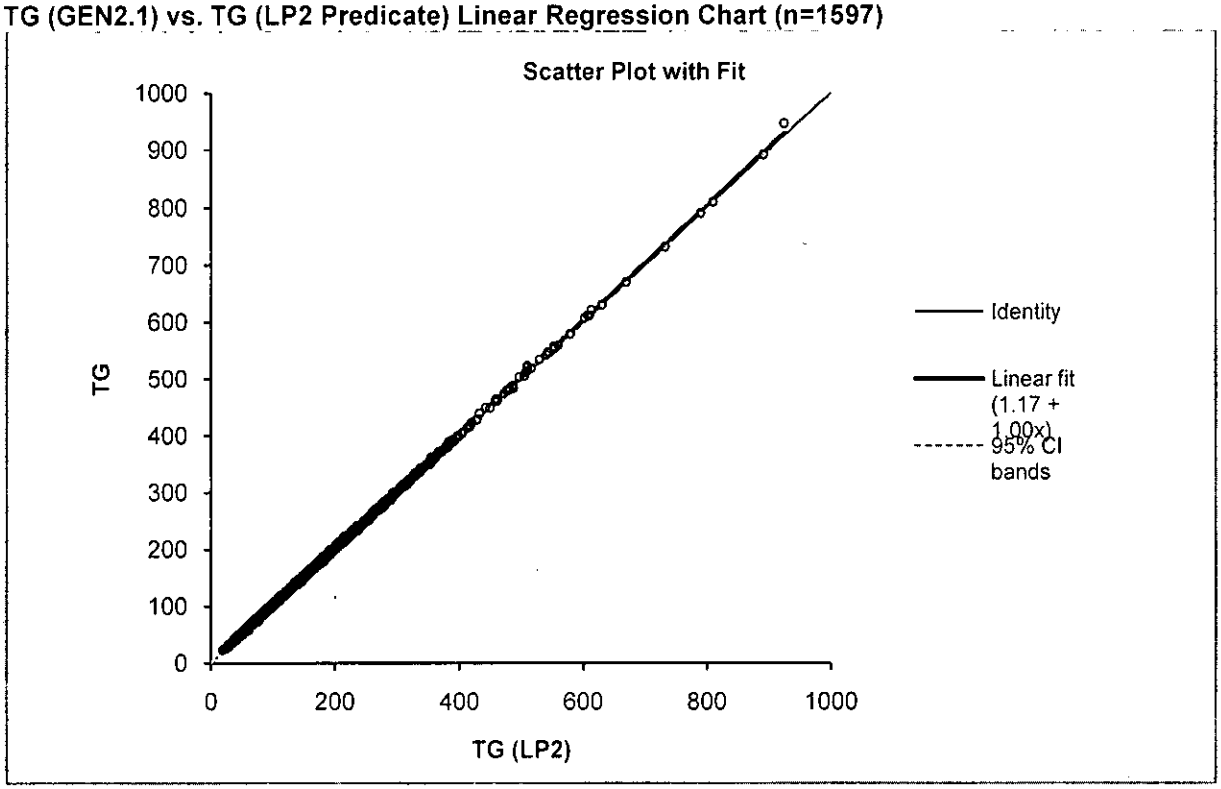


Linear regression analysis: y = 1.00x +0.03 r = 0.999

Method comparison Triglycerides

Method comparison was evaluated by using serum samples across the reportable range of the *NMR LipoProfile* test for Triglycerides on the NMR Profiler. Triglyceride concentrations ranged from 20 to 925 mg/dL.

TG (GEN2.1) vs. TG (LP2 Predicate) Linear Regression Chart (n=1597)



Linear regression analysis: y = 1.00x +1.17 r = 1.00

K. Standard/Guidance Document Referenced (if applicable):

Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices.

CLSI EP5-A2. Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline.

CLSI EP9-A2. Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline.

CLSI EP17-A. Protocols for Determination of Limits of Detection and Limits of Quantitation; Approved Guideline.

CLSI EP6-A. Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline.

CLSI C28-A3. Defining Establishing, and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline

This device has not been tested by the Cholesterol Reference Method Laboratory Network.

M. Clinical Studies:

a. Clinical Sensitivity:

Not Applicable

b. Clinical specificity:

Not Applicable

c. Other clinical supportive data (when a. and b. are not applicable):

Not Applicable

1. Clinical cut-off:

Not Applicable

2. Expected values/Reference range:

Distribution of LDL-P Observed in a Reference Population – Multi-Ethnic Study of Atherosclerosis (MESA)

	All (n=5,362)	**Men** (n=2,529)	**Women** (n=2,833)
Percentile	**LDL-P** (nmol/L)	**LDL-P** (nmol/L)	**LDL-P** (nmol/L)
5	770	800	760
10	870	900	850
20	1000	1040	970
30	1100	1150	1060
40	1190	1250	1150
50	1280	1330	1230
60	1380	1430	1330
70	1480	1530	1440
80	1610	1640	1570
90	1790	1820	1760
95	1980	1990	1970

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration

10903 New Hampshire Avenue
Silver Spring, MD 20993

LipoScience, Inc.
c/o Suzette Warner
Regulatory Affairs Manager
2500 Sumner Boulevard
Raleigh, NC 27616

SEP 27 2011

Re: k111516
Trade/Device Name: NMR LipoProfile Test and NMR Profiler
Regulation Number: 21 CFR 862.1475
Regulation Name: Lipoprotein Test System
Regulatory Class: Class I, subject to limitation of exemption in 21 CFR 862.9(c)(4)
Product Code: MRR, LBS, CDT
Dated: August 11, 2011
Received: August 15, 2011

Dear Ms. Warner:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into class II (Special Controls), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820). This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 796-5450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding postmarket surveillance, please contact CDRH's Office of Surveillance and Biometric's (OSB's) Division of Postmarket Surveillance at (301) 796-5760. For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-5680 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

Indications for Use Form

510(k) Number: k111516

Device Name: *NMR LipoProfile*® test and NMR Profiler

Indications for Use:

The *NMR LipoProfile*® test, when used with the NMR Profiler, an automated NMR spectrometer, measures lipoprotein particles to quantify LDL particle number (LDL-P), HDL cholesterol (HDL-C), and triglycerides in human serum and plasma using nuclear magnetic resonance (NMR) spectroscopy. LDL-P and these NMR-derived concentrations of HDL-C and triglycerides are used in conjunction with other lipid measurements and clinical evaluation to aid in the management of lipoprotein disorders associated with cardiovascular disease. This test is performed and provided as a service by LipoScience Laboratory.

Prescription Use X (Part 21 CFR 801 Subpart D) AND/OR Over-The-Counter Use _____ (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE OF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Division Sign-Off
Office of In Vitro Diagnostic Device
Evaluation and Safety
510(k) k111516